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# Building foundations for transcatheter intervascular anastomoses: 3D anatomy of the great vessels in large experimental animals

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## Abstract

**OBJECTIVES:** To provide comprehensive illustrations of anatomy of the relevant vessels in large experimental animals in an interactive format as preparation for developing an effective and safe transcatheter technique of aortopulmonary and bidirectional cavopulmonary intervascular anastomoses.

**METHODS:** Computed tomographic angiographic studies in two calves and two sheep were used to prepare 3D reconstructions of the aorta, pulmonary arteries, and caval and pulmonary veins. Based on these reconstructions, computer simulations of the creation of stent-enhanced aortopulmonary and bidirectional cavopulmonary anastomoses were made.

**RESULTS:** We observed the following major anatomical features: (i) caudal course of the main pulmonary artery and its branches with the proximal right pulmonary artery located immediately caudal to the aortic arch, and with the central left pulmonary artery lying at a substantial distance from the descending aorta; and (ii) the distal right pulmonary artery is located dorsal to the right atrium and inferior caval vein at a substantial distance from the superior caval vein. Animations showed creation of transcatheter analogues of Waterston's and Potts' aortopulmonary shunts through placement of a covered spool-shaped stent, and the transcatheter creation of bidirectional Glenn's cavopulmonary anastomosis, by placement of a long covered trumpet-shaped stent.

**CONCLUSIONS:** There are considerable differences in vascular anatomy between large experimental animals and humans. Given the need to elaborate new transcatheter techniques for intervascular anastomoses in suitable animal models before application to human, it is crucial to take these anatomical differences into account during testing and optimization of the proposed procedures.

**Keywords:** Stent • Aortopulmonary shunt • Cavopulmonary anastomosis • Vascular anatomy • Experimental animals

## INTRODUCTION

Several intervascular shunt procedures have become standard techniques in the treatment of patients with severe congenital heart disease. The first step in the management of severe right ventricular outflow tract obstruction is, in general, a systemic-to-pulmonary artery anastomosis, with the modified Blalock–Taussig shunt, using a polytetrafluoroethylene graft, being mostly performed. Patients with univentricular heart defects or those with borderline right ventricular hypoplasia mostly undergo the bidirectional superior cavopulmonary connection procedure (Glenn anastomosis), as a halfway stage to completion of the univentricular palliation, or as a so-called 'one-and-a-half ventricular repair'. Both types of anastomosis are currently performed surgically, and are associated with substantial morbidity and even mortality [1, 2]. Together with other operations needed to achieve optimal correction of the haemodynamics, initial palliative shunt procedures considerably contribute to the misfortunes of multiple cardiothoracic surgeries. Very recently, a clinical

interest has emerged in the descending aorta to left pulmonary artery anastomosis as a potential palliative management in cases of therapy-resistant suprasystemic pulmonary arterial hypertension [3], where surgical procedures are associated with high risk.

Transcatheter procedures have lower risk of complications, shorter hospital stay and do not need cardiopulmonary bypass or opening of the chest. Thus, the endovascular approach to create an intervascular anastomosis is a very attractive concept. However, before applying the idea of anastomosing two adjacent vessels through a transcatheter approach in humans, such a technique should be carefully elaborated in a suitable model of congenital heart defects or pulmonary hypertension in large experimental animals, where a thorough understanding of the related vascular anatomy is of crucial importance. Although some reports described the technical feasibility of transcatheter creation of intervascular anastomoses in normal dogs and pigs [4–7], their major setback is the nearly complete lack of anatomical reasoning of such interventions. Besides the lack of the suitable large animal

models, information about the exact relations between caval veins, pulmonary arteries and the aorta in large domestic animals is very scarce. However, such anatomical details are crucial for optimal procedure planning. To build the foundations for application of this potential novel interventional technique finally in humans, we sought to characterize the 3D anatomy of the great vessels in living calves and sheep. These large domestic animals have a cardiac physiology that is almost identical to humans and are used increasingly as experimental models in cardiovascular device testing. Here, we present the findings of considerably different animal vascular anatomy, when compared with human, in an interactive portable document format, and the computer simulations of anatomical aspects of the transcatheter aortopulmonary and cavopulmonary anastomoses in large experimental animals.

## MATERIALS AND METHODS

### Computed tomographic angiography

Four animals (3-week old calf, 3-month old calf, 4-month old sheep and 5-year old sheep) were studied under general inhalational anaesthesia by computed tomography (CT) performed using a 40-slice scanner (Somatom Sensation Open, Siemens). Subsequent to a native scan of the thorax, a contrast medium (Ultravist®-370, Bayer Schering Pharma) was injected intravenously in three animals. In one animal, only native CT was performed twice, at the age of 4 and 7 months. Images were acquired from the thoracic inlet to the cranial abdomen. Data were reconstructed with a soft tissue algorithm to images with 1.5-mm slice thickness and stored in the DICOM format.

In animals, the official terms for the systemic veins entering the heart are cranial and caudal caval veins [8]. However, here we use the terms superior and inferior to facilitate comparison of our findings with human cardiovascular anatomy well described elsewhere. The terms cranial/caudal and ventral/dorsal pertain to the rest of the anatomical descriptions as generally used in veterinary anatomy. The small number of animals used in this study is a limiting factor not allowing quantitative comparisons between sheep and calves or between human and large experimental animals.

### Three-dimensional reconstructions

For preparing the morphological 3D models of the vessels, the images of serial CT angiography data, after converting from the DICOM to bitmap format, were loaded into the Amira software. The label fields were manually created for the walls of both caval veins and the adjacent right atrium (colour coded as blue); the aorta and brachiocephalic trunk (red); the main pulmonary artery and its branches (purple); and for the lumen of pulmonary veins and the adjacent left atrium (orange). After correction of deformities in the label fields, the 3D surface was generated, simplified and further smoothed. For the interactive 3D-PDF file, the 3D surfaces were exported from Amira into Adobe Acrobat using procedures described elsewhere [9].

### Simulations of transcatheter anastomoses

To create animations, the 3D surfaces generated in Amira were exported as Stanford files and imported into the Blender software. Using the imported data as a template, the 3D models were

recreated in Blender resulting in smooth, low polygon-number models. The simulation of wire, catheter and intervascular stents, and also the supposed alteration of vascular anatomy were produced using the relative shape keys tool. The resulting animations were exported into AVI format video files and incorporated into one PDF file, available in the [Supplementary Data](#).

## RESULTS

The reader is encouraged to read the results along with the interactive 3D-PDF file.

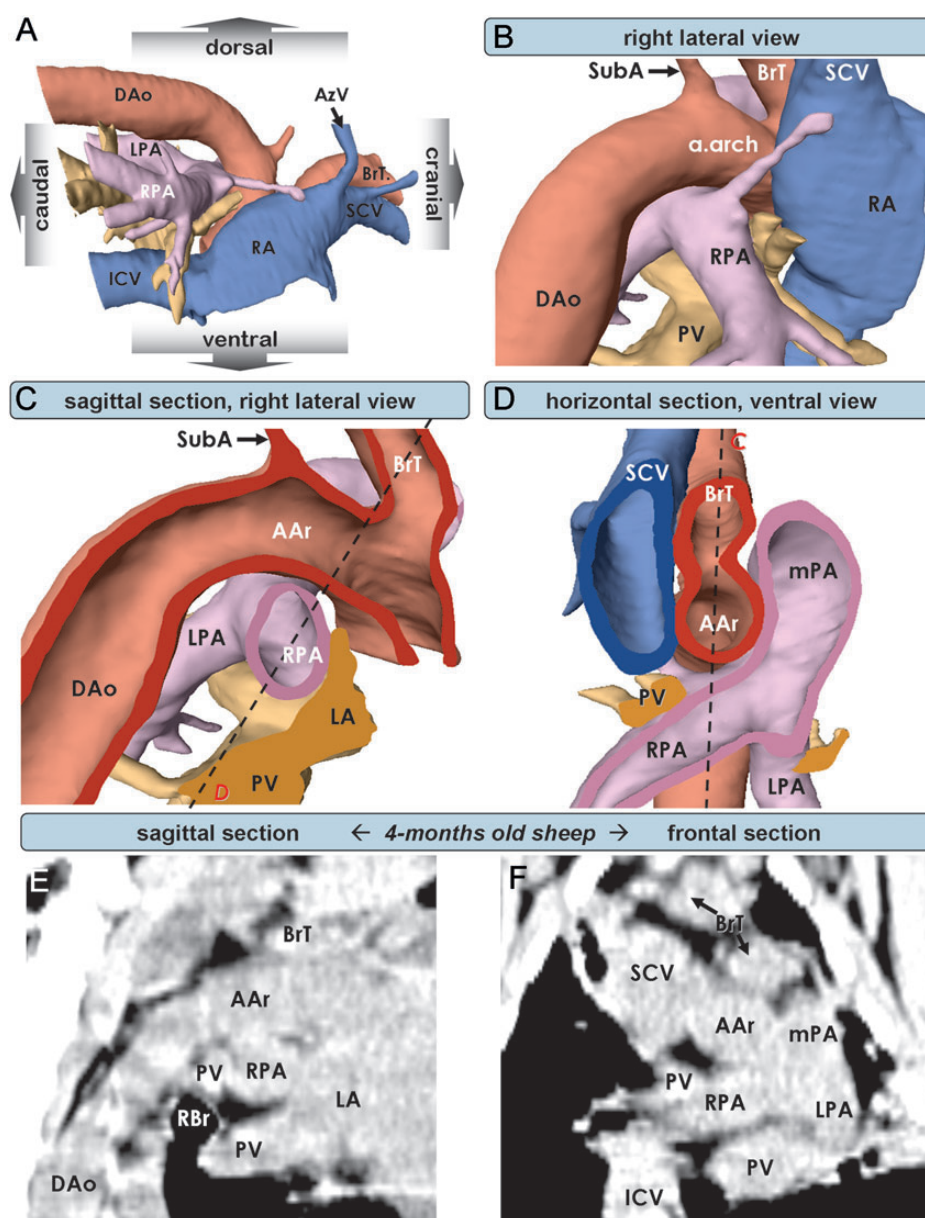
### Vascular anatomy in relation to aortopulmonary anastomoses

We observed several differences regarding vascular anatomy between domestic animals and humans. In calves and sheep, the ascending aorta is much shorter and courses mainly dorso cranially, representing the proximal part of the aortic arch. From the aortic arch emerges only one branch, the brachiocephalic trunk. The aortic arch continues as the descending aorta running caudally (Figs 1A–C and 2A). Perpendicularly and left to the ascending aorta, the main pulmonary artery traverses from the right ventricle into the dorsal direction (Figs 1C and 2A and B). The trunk of the main pulmonary artery is considerably longer than the ascending aorta and has a curved shape, with the distal part running caudally in close proximity to the aortic arch. At the level of the caudal surface of the aortic arch, the main pulmonary artery bifurcates into the right and left branches, which run caudally and to both lateral sides (Figs 1B, C and D and 2B and C). The most proximal part of the right pulmonary artery lies immediately under the aortic arch, with almost no free space between their walls (Fig. 1C–F), whereas there is a substantial distance between the right pulmonary artery and the ascending aorta. The left pulmonary artery runs almost parallel to the descending aorta, with considerable distance between their walls in this limited number of analysed animals, but without interposing lung tissue (Fig. 2B–F).

### Simulation of transcatheter creation of the aortopulmonary anastomoses

The transcatheter analogues of the Waterston's ascending aorta to right pulmonary artery anastomosis and the Potts' descending aorta to left pulmonary artery shunt procedures seem the most attractive aortopulmonary anastomoses to be created endovascularly. As has been shown, use of a spool-shaped covered stent considerably facilitates the safe and stable communication between two vessels [4, 10]. The flaring ends of the stent are fixed tightly between the adjacent vascular walls, creating a hermetic aortopulmonary communication of known diameter. In our simulations, we demonstrated placement of the covered spool-shaped stent with the diameter of the anastomosing part of ~4 mm. Perforation of the vascular walls, insertion of catheters and introduction of the spool-shaped stent are proposed to be performed from the aorta towards the pulmonary arterial side.

Given the above-described anatomical features, the most optimal place for the transcatheter Waterston's anastomosis in calf or sheep was between the proximal part of the central right pulmonary artery and the middle portion of the aortic arch. Animation 1 (see



**Figure 1:** Vascular anatomy related to the transcatheter Waterston's aortopulmonary anastomosis. (A) Right lateral view of the vessels as seen within the thorax of an upright-standing animal. To facilitate comparison with human anatomy, the views in panels (B–F) are adapted. Note identical anatomical features in the 3-week old calf (C and D) and in the 4-month old sheep (E and F). For further description, see text. AAr: aortic arch; AzV: azygos vein; BrT: brachiocephalic trunk; DAo: descending aorta; mPA: main pulmonary artery; PV: pulmonary vein; RA/LA: right/left atrium; RBr: right bronchus; RPA/LPA: right/left pulmonary artery; SubA: sub clavian artery; SCV/ICV: superior/inferior caval vein.

[Supplementary Data](#)) demonstrates a very simplified sequence of perforating the caudal wall of the aortic arch with protrusion of the wire through the intervascular space, and perforating the cranial wall of the right pulmonary artery. Then, a catheter containing the self-expanding spool-shaped covered stent was advanced from the lumen of the aortic arch into the lumen of the proximal right pulmonary artery and the stent was deployed between the two vessels, resulting in a Waterston's aortopulmonary anastomosis (Fig. 3A–C).

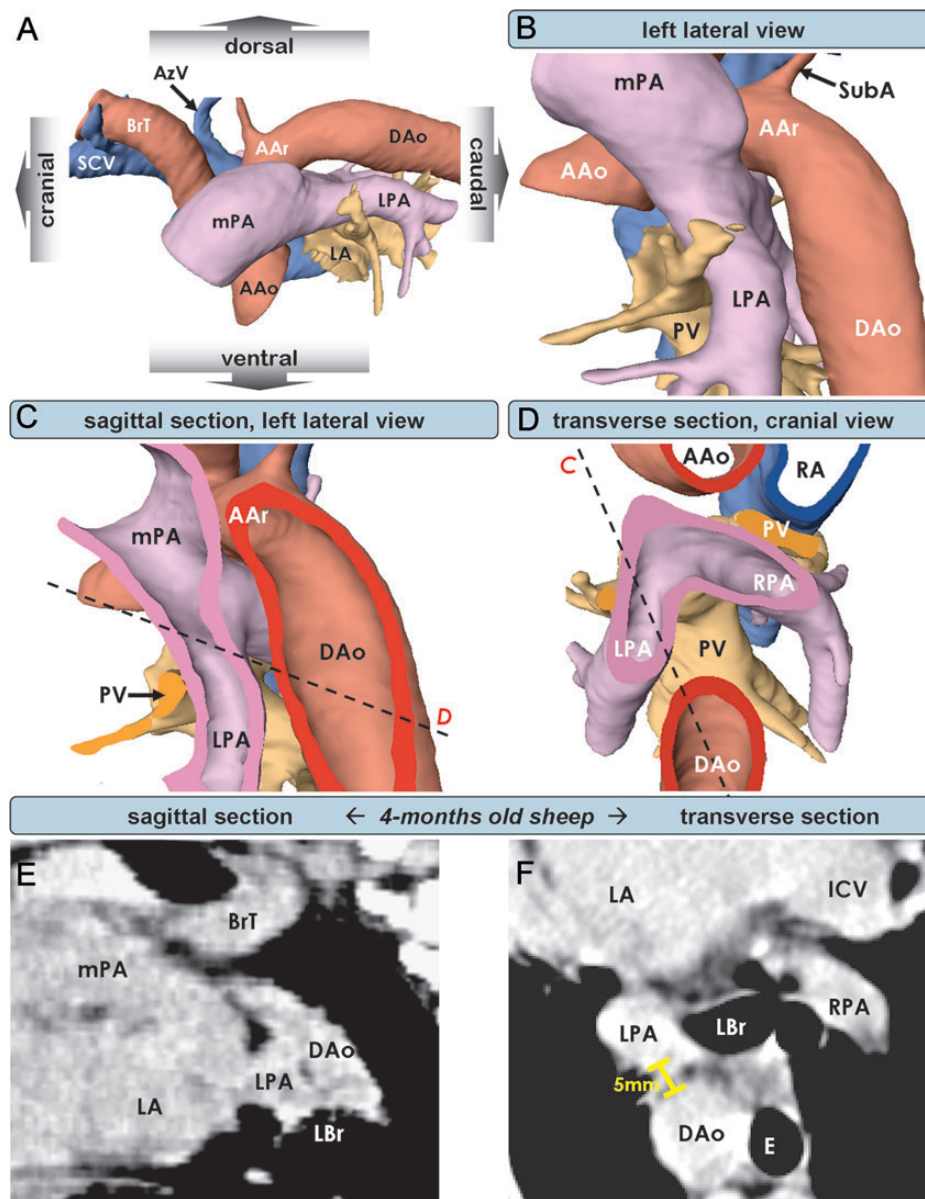
The creation of the transcatheter Potts' anastomosis in calf or sheep is probably more challenging than it would be in humans, due to the substantial distance between their walls. The place between the distal part of the central left pulmonary artery, just before its branching, and the opposite descending aorta seems the most optimal. Animation 2 shows a simplified sequence of perforating the ventral wall of the descending aorta with protrusion of the

wire through the intervascular space, and perforating the dorsal wall of the left pulmonary artery. Then, a catheter containing the self-expanding spool-shaped covered stent was advanced from the lumen of the descending aorta into the lumen of the left pulmonary artery and the stent was deployed between the two vessels, resulting in a Potts' aortopulmonary anastomosis (Fig. 3D–F). The predicted vascular wall displacements due to implantation of the stent between two adjacent vessels are shown.

### Vascular anatomy in relation to the bidirectional superior cavopulmonary anastomosis

The position of the right pulmonary artery in relation to the superior caval vein in calf and sheep differs remarkably from that in





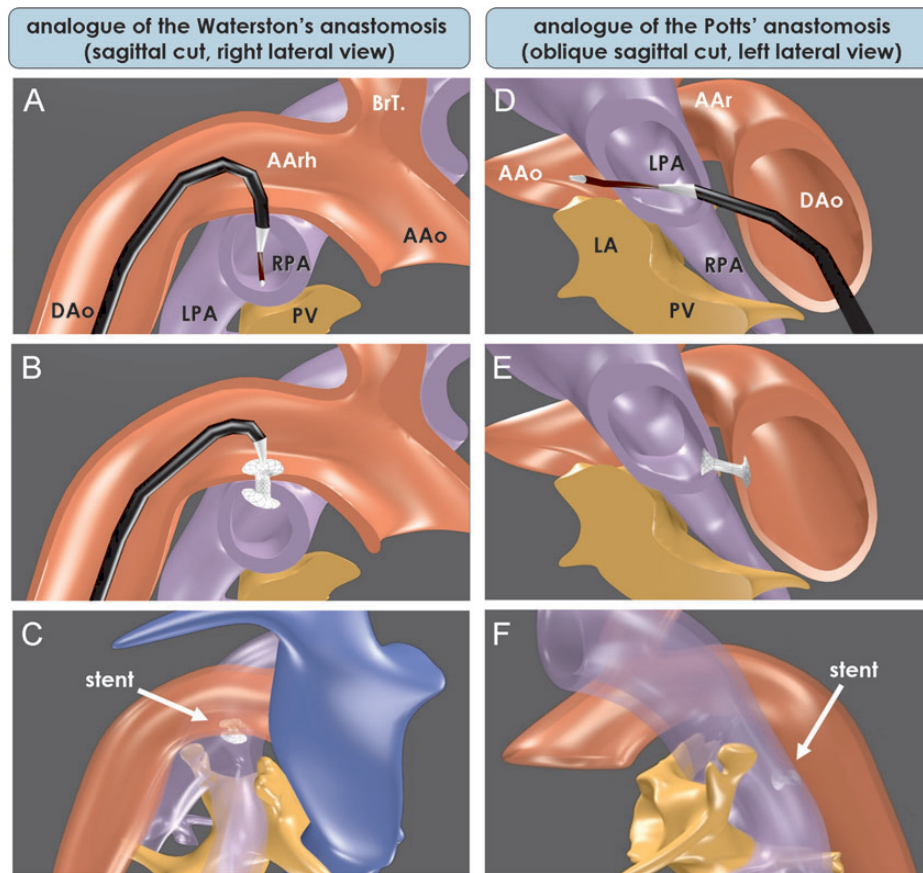
**Figure 2:** Vascular anatomy related to the transcatheter Potts' aortopulmonary anastomosis. (A) Left lateral view of the vessels as seen within the thorax of an upright-standing animal. To facilitate comparison with human anatomy, the views in panels (B–F) are adapted. Anatomical features in the 3-week old calf (C and D) and the 4-month old sheep (E and F) are identical. For further description, see text. E: oesophagus; LBr: left bronchus; AzV: azygos vein; BrT: brachiocephalic trunk; SCV: superior caval vein; mPA: main pulmonary artery; AAr: aortic arch; RA: right atrium; PV: pulmonary vein; RPA/LPA: right/left pulmonary artery; DAo: descending; ICV: inferior caval vein.

humans. In domestic animals, the main pulmonary artery and its branches run dorso caudally almost parallel to the dorsal wall of the atria (Fig. 1A and B). The distal part of the central right pulmonary artery runs behind the junction of the inferior caval vein with the right atrium (Fig. 4A and B). This results in a long distance between the walls of the superior caval vein and right pulmonary artery, which is ~2–2.5 cm in 4- to 7-month old sheep (Fig. 4E–H). Furthermore, in contrast to humans, the angle between the right pulmonary artery and the superior caval vein is oblique (Fig. 4D). In the space between the right atrium and right pulmonary artery run the right pulmonary veins (Fig. 4A–D). The superior caval vein joins the right atrium with substantial offset relative to the orifice of the inferior caval vein (Fig. 4C). The offset between the

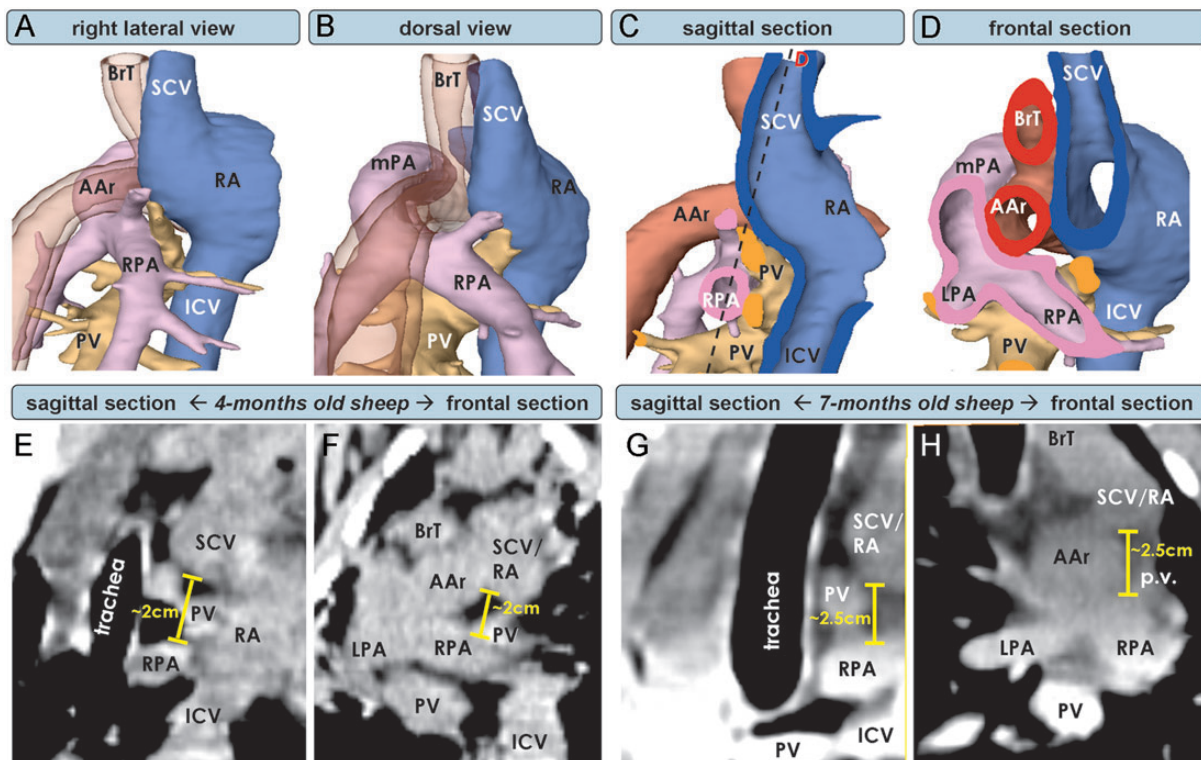
junctions of the superior and inferior caval veins with the right atrium is even larger in 5-year old sheep (Fig. 5). In such an older animal, the inferior caval vein is the closest large systemic venous structure to the right pulmonary artery.

### Simulation of transcatheter creation of the bidirectional superior cavopulmonary anastomosis

In sheep and calf, the dorsal wall of the right atrium and the most distal part of the inferior caval vein are in relatively close proximity to the right pulmonary artery, not the superior caval vein (Fig. 4C and D). These anatomical features make direct anastomosing of the superior caval vein with the right pulmonary artery in these

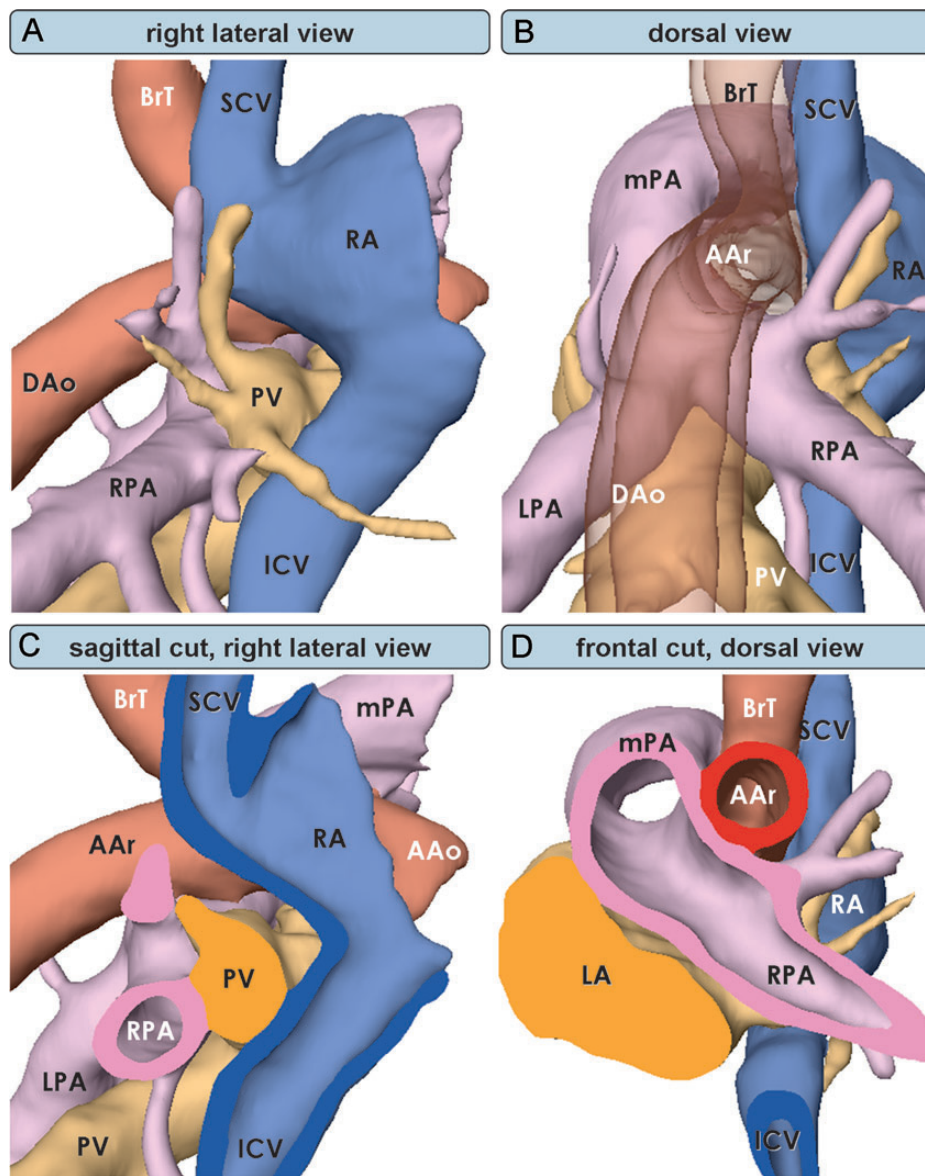


**Figure 3:** Snapshots from animations showing anatomical aspects of the transcatheter aortopulmonary anastomoses using a spool-shaped covered stent. For further description, see text. BrT: brachiocephalic trunk; RPA/LPA: right/left pulmonary artery; DAo: descending; PV: pulmonary vein; AAr: aortic arch.



**Figure 4:** Vascular anatomy related to the transcatheter bidirectional Glenn-like anastomosis. Note the long distance between the superior caval vein and right pulmonary artery, as seen in the 3-month old calf (A–D) and the 4- to 7-month old sheep (E–H). For further description, see text. BrT: brachiocephalic trunk; RPA/LPA: right/left pulmonary artery; SCV/ICV: superior/inferior caval vein; RA: right atrium; AAr: aortic arch; mPA: main pulmonary artery; PV: pulmonary vein.

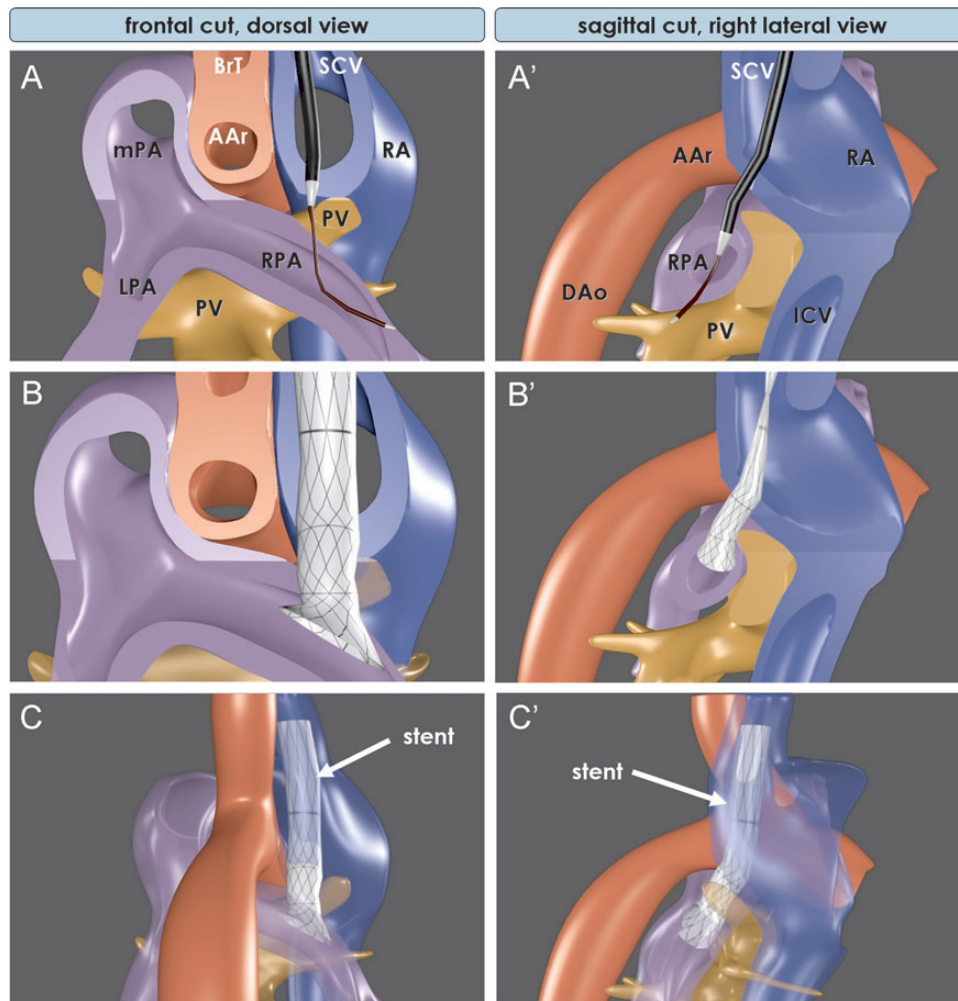




**Figure 5:** Vascular anatomy in a 5-year old sheep. Note the substantial offset between the orifices of superior and inferior caval veins (**A** and **C**). In older animals, the distal part of the central right pulmonary artery is even closer to the inferior caval vein, which would allow the transcatheter creation of an anastomosis between these two vessels. BrT: brachiocephalic trunk; SCV/ICV: superior/inferior caval vein; mPA: main pulmonary artery; AAr: aortic arch; RA: right atrium; PV: pulmonary vein; RPA/LPA: right/left pulmonary artery; DAo: descending.

experimental animals impossible. Anastomosis of the right atrium with the right pulmonary artery using a spool-shaped stent results in massive leakage of the caval venous blood to the right atrium [11]. To resolve this problem, we propose to use the trumpet-shaped long covered stent, with only one end flaring within the lumen of the right pulmonary artery, while the other non-flaring end rests within the superior caval vein. Such a long covered stent creates an intra-atrial tunnel, directing all the blood from the upper body to both lungs. In our simulation of the transcatheter analogue of bidirectional cavopulmonary anastomosis, we demonstrated the placement of such a stent with a diameter of  $\sim 10$  mm. Perforation of the walls of the right atrium and right pulmonary artery, insertion of a catheter between these two compartments and introduction of the stent are proposed to be performed from the cranially located superior caval vein towards the caudally located right pulmonary artery.

Animation 3 demonstrates the simplified sequence of perforating first the dorso caudal wall of the right atrium with protrusion of the wire through the intervascular space, and penetrating the cranial wall of the right pulmonary artery. Then, a catheter containing the self-expanding trumpet-shaped covered stent was advanced from the lumen of the right atrium into the lumen of right pulmonary artery, and the stent was deployed between two compartments. The distal end of the expanding stent was flaring within the right pulmonary artery, hereby fixing the stent tightly within its lumen and allowing blood flow from the stent to both pulmonary arteries. The long proximal end of the stent expanded within the lumen of the right atrium and the distal superior caval vein (Fig. 6). This resulted in a bidirectional superior cavopulmonary anastomosis. The predicted vascular deformations due to implantation of the stent are simulated.



**Figure 6:** Snapshots from an animation showing anatomical aspects of the transcatheter bidirectional Glenn anastomosis using a trumpet-shaped covered stent. For further description, see text. BrT: brachiocephalic trunk; SCV/ICV: superior/inferior caval vein; mPA: main pulmonary artery; AAr: aortic arch; RA: right atrium; PV: pulmonary vein; RPA/LPA: right/left pulmonary artery; DAo: descending.

## DISCUSSION

Searching for safer palliation in patients with severe portal hypertension resulted in the concept of the transcatheter construction of transjugular intrahepatic portosystemic shunt [12]. Given technical challenges and frequent complications of the intrahepatic shunt, the transcatheter extrahepatic portocaval anastomosis using A spool-shaped covered stent was proposed and shown to be technically possible [4, 10, 13–15]. Together with an extrahepatic portocaval shunt, transcatheter aortopulmonary and cavo-pulmonary anastomoses using sophisticated equipment with a kinematic needle were reported to be successful in normal dogs [4, 11]. The feasibility of the transcatheter creation of such intervascular communications using a less complex approach of radiofrequency energy-induced perforation was recently tested in the pig [5–7]. Intuitively, endovascular perforation of the walls of two adjacent vessels with passing the catheters between them can easily cause bleeding and vessel damage. Nonetheless, it has been shown that, in the case of appropriate performance, the bleeding is minimal or absent, with no vascular rupture. As has been demonstrated very recently in adult patients with severe pulmonary hypertension [16],

and previously in dogs [4, 11], the proper fixation of both ends of the stent within the two adjacent vessels is the major factor contributing to the safe outcome of the transcatheter intervascular anastomosis procedure. Moreover, optimal and purpose-focused design of the stents used to create the different intervascular anastomoses also seems to be of influence.

Comprehensive understanding of the anatomy of the heart and great vessels in experimental animals, which are increasingly used in the development and testing of diverse cardiovascular devices and interventions, is of crucial importance. The existing descriptions of cardiovascular anatomy in large domestic animals concentrate mainly on the intracardiac features and topographic anatomical aspects of the vessels. Herewith, there are almost no illustrations of the large arteries and caval veins, which would allow analysis of the anatomical feasibility of the relatively novel technique of transcatheter intervascular anastomoses. In our study, we tried to fill this gap by characterizing the exact relations between central vascular structures in young calves and sheep and by relating our findings to the transcatheter analogues of aortopulmonary and superior cavopulmonary anastomoses.



## Aortopulmonary anastomoses

The close proximity of the central pulmonary arteries to the different parts of the aorta enabled surgeons in the past to create different types of central aortopulmonary anastomoses with the aim to palliate severe cyanotic heart defects. Two particular procedures, Waterston's ascending aorta to right pulmonary artery anastomosis and Potts' descending aorta to left pulmonary artery shunt, became widely used, but because of serious complications were discarded and replaced by the modified Blalock-Taussig shunt. However, these complications, excessive left-to-right shunt, pulmonary arterial hypertension and pulmonary artery deformities, were, almost entirely due to the redundant diameter of the anastomoses and the technical difficulties of suturing adjacent walls of the pulmonary artery and aorta together through the lateral thoracotomy [17, 18]. Perforating the walls of these vessels and placing the anastomosing stent endovascularly in the setting of unaltered vascular anatomy will avoid the problems of pulmonary artery deformities related to the surgical approach. With choosing the appropriately sized stent, the problems of excessive pulmonary blood flow can be avoided as well.

In large domestic animals, compared with humans, there are considerable differences in the anatomy of related vessels. Thus, the transcatheter analogue of a Waterston's anastomosis in calf or sheep is best to create between the aortic arch and the proximal right pulmonary artery, whereas, in the case of a Potts' shunt, the central left pulmonary artery is closest to the descending aorta at its distal part. The distance between the descending aorta and the left pulmonary artery is, possibly, a matter of anatomical variation, as has been reported in a study on adult patients with severe pulmonary hypertension [19]. In calf and sheep, the ascending aorta lies at a substantial distance from the right pulmonary artery, but in very close proximity with the main pulmonary artery trunk. The close proximity of these two vessels makes the creation of an anastomosis between them possible by an endovascular approach, as has been demonstrated in pig [6]. The procedure of a transcatheter analogue of such a central aortopulmonary anastomosis will be identical to the technique of the Waterston's shunt described above.

## Bidirectional superior cavopulmonary anastomosis

Although the creation of aortopulmonary anastomoses by the endovascular approach seems relatively straightforward, anastomosing the right pulmonary artery with the superior caval vein by using the same technique in pigs appeared much more technically challenging [5, 7]. The findings of our study elucidate the anatomical reasons of these difficulties. In large domestic animals, the course of the superior caval vein and the right pulmonary artery is unsuitable for direct anastomosis of these vessels, as has been proved in experiments testing mechanical cavopulmonary assist device in a newborn piglet model of the bidirectional Glenn anastomosis [20]. The anastomosis between the central right pulmonary artery and the dorsal wall of the right atrium using a spool-shaped stent in dog did not separate caval venous blood from the right atrial cavity, although it resulted in a bidirectional flow of systemic venous flow to the pulmonary circulation [4, 11]. The placement of the long covered stent, directly from the superior caval vein through the right atrial cavity into the right pulmonary artery avoided leakage of the caval blood to the right atrium,

but resulted in a unidirectional cavopulmonary anastomosis with caval blood flow only to the right lung [5, 7]. These approaches can be combined in a trumpet-shaped long covered stent to achieve a haemodynamically favourable bidirectional superior cavopulmonary anastomosis in a large experimental animal. The flaring distal end of such a stent will provide the bidirectionality of blood flow, whereas the long non-flaring proximal end of the covered stent will direct the superior caval venous blood directly to the pulmonary circulation. In sheep and calf, due to considerable distance between the most distal superior caval vein and the proximal pulmonary artery, the penetrating wire and the trumpet-shaped stent will be during placement in close proximity to the upper right pulmonary vein, but not to the main right bronchus (Fig. 4). However, our limited data and previous reports of uncomplicated stent-enhanced cavopulmonary anastomosis in pig [5, 7] suggest that this is not a limiting factor.

A high percentage of thrombosis within the long covered stents used to create the cavopulmonary anastomosis in pig was assigned to the low amount of blood coming from the small porcine brain. In fact, data on caval blood flow quantification in animals are scarce. In adult miniature pigs and mongrel dogs, the superior caval venous flow was reported to be ~33 ml/kg/min with a superior caval venous flow fraction of the total cardiac output being about one-third [21, 22]. These data indicate that, in adult large experimental animals, the superior caval venous flow is less than that in human infants and young children [23], which could possibly contribute to thrombogenicity of large covered stents in cavopulmonary connections. However, there are no quantitative data on caval venous flow in young postnatal animals, where superior caval flow can be higher.

The ultimate goal of univentricular palliation is completion of the total cavopulmonary connection, where all systemic venous blood is directed into the pulmonary arteries bypassing the heart. Transcatheter total isolation of the caval venous blood flow from the cavity of the right atrium by deployment of a long covered stent between the orifices of both caval veins in pig and sheep is technically feasible [24, 25]. However, this approach will be unsuitable after applying the transcatheter technique of the bidirectional Glenn anastomosis proposed in our study. Nonetheless, the close proximity of the distal inferior caval vein to the right pulmonary artery in older animals suggests that a similar procedure of transcatheter placement of the trumpet-shaped covered stent between these two vessels could be used to complete the total cavopulmonary connection in the same experimental animal. Discussion on interventional options for eliminating either native or artificial antegrade pulmonary blood flow goes beyond the scope of this report.

## CONCLUSIONS

There are considerable differences in vascular anatomy in large experimental animals, when compared with humans. Given the need to elaborate new transcatheter techniques of intervascular anastomoses in suitable animal models before application to human patients, it is crucial to take these anatomical differences into account during testing and optimization of the proposed procedures. Although there are many technical, haemodynamical and clinical aspects to be addressed in future studies, choosing the most optimal sites and stent designs lays the foundation for successful endovascular creation of intervascular anastomoses.

## SUPPLEMENTARY MATERIAL

Supplementary material is available at *ICVTS* online.

## ACKNOWLEDGEMENTS

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**Conflict of interest:** none declared.

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